192 Inhibition of Peptidases Potentiates Enkephalin-Induced Contraction of Gastric Muscle Cells

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Cell-surface peptidases degrade enkephalins and thereby restrict the number of molecules available to activate receptors. The effects of peptidase inhibitors on the degradation and contractile actions of enkephalin on gastric smooth muscle cells were examined. Muscle cells were isolated from the guinea-pig by collagenase digestion. Cells degraded [Tyr[1]-^{3}H][Leu[5]]enkephalin (assessed by reverse-phase HPLC): 29 ± 1% degradation, 30 min incubation; 53 ± 0.5%, 60 min; 76 ± 4%, 120 min (mean ± SD, n = 3 animals). Amastatin (10 μM, aminopeptidase inhibitor) inhibited degradation by 72 ± 1% (n = 4). Residual activity was inhibited by phosphoramidon (1 μM, endopeptidase EC 3.4.24.11 inhibitor) by 58 ± 11% (n = 4). Presence of EC 3.4.24.11 was confirmed by indirect immunocytochemistry. Enkephalin stimulated contraction of cells (assessed by microscopy after a 30 s incubation) in a dose-related manner (EC_{50} 10 ± 0.4 μM, n = 3). Pre-treatment of cells with amastatin (10 μM) plus phosphoramidon (1 μM) increased the potency of enkephalin 100-fold (EC_{50} 0.9 ± 0.3 nM, n = 3). The efficacy of the contractile response was unchanged by the inhibitors (22 ± 0.5%, controls: 22 ± 0.6% with inhibitors; % decrease in cell length, n = 3). Gastric muscle cells degrade enkephalins by the action of aminopeptidases and EC 3.4.24.11. These peptidases modulate the biological actions of enkephalins. The rapidity and magnitude of the potentiating effects of the inhibitors suggests a close relationship between the peptidases and the enkephalin receptor.

193 The Effect of the Long Acting Somatostatin Analogue (SMS 201–995) in the Treatment of Beta Cell Tumors of the Pancreas

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The long acting somatostatin analogue (SMS 201–995, Sandostatin, Sandoz, Basel) was applied in the preoperative management of 5 patients (3 female and 2 male; mean age: 50 ± 10 years; BMI: 27 ± 2.8 kg/m^2) with organic hyperinsulinism (subsequently confirmed during surgery as 4 adenomas and 1 carcinoma of the beta cells of the pancreas) in two different doses: 3 × 50 μg s.c. daily from day 1 to day 7 and 4 × 100 μg s.c. daily from day 8 to day 15. On day 0 (placebo) 24-h profile of glycaemia (glucose oxidase), insulin (RIA INEP) and C-peptide (RIA Biodata) was done. During SMS 201–995 application the same parameters were followed at 6, 9, 12, 15, 18, 21 and 24 h from day 2 to day 15. Glucagon (RIA Biodata) was determined hourly, from 8 to 18 h, on day 0, 1, 8 and 15. During the treatment course with 3 × 50 μg a fall in the mean plasma insulin levels was registered in adenoma patients (70, 63, 80 and 40%, respectively) and only 9% in the patient with carcinoma. Further increase to 4 × 100 μg leads to less suppression in the mean plasma insulin levels in adenoma patients (52, 43, 46 and 17%, respectively) and a greater fall in the patient with carcinoma (47%). The values of the C-peptide were similar to plasma insulin values. SMS 201–995 administration elevates plasma glucose in 3 adenoma patients and in the patient with carcinoma while in one patient with adenoma no change in plasma glucose was found, independent of the dose used. The plasma glucagon levels were low normal.

In conclusion, the administration of SMS 201–995 in the preoperative management of patients with beta cell tumors of the pancreas leads to significant suppression in insulin secretion and improvement in plasma glucose values and clinical symptoms.

194 Postprandial Glucagon-Like Peptide-1 (GLP-1), Enteroglucagon and Emptying of the Gastric Substitute after Total Gastrectomy

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Postprandial hyperinsulinemia, and reactive hypoglycemia in some cases, is a well known phenomenon in patients after total gastrectomy, particularly in those suffering from the dumping syndrome. It was the purpose of this study to shed light on the relationship between rapid emptying of the gastric substitute, the insulinotropic glucagon-like peptide-1 (GLP-1) and postprandial dumping. Postprandial GLP-1, enteroglucagon, and insulin were measured by radioimmunoassay in 27 tumour-free patients 49 months (median) after total gastrectomy and in 4 controls. A ^{99m}Technetium-labeled 100 g carbohydrate solid test meal was used to measure emptying of the gastric substitute by scintigraphy in 18 patients. 14 patients suffered from the dumping syndrome, and the intensity of postprandial dumping symptoms (Sigstad's diagnostic index) correlated with early (first 30 min) integrated GLP-1, enteroglucagon and insulin. The peak concentration of GLP-1 was measured at 15 min, peak insulin 30 min after the end of the meal. The peak GLP-1 concentration was 284 ± 40 pmol/l [mean ± SE] in dumpers, significantly ($p < 0.05$) higher than in non-dumpers (137 ± 19 pmol/l) and in controls (40 ± 20 pmol/l). The peak insulin concentration was 839 ± 161 pmol/l in dumpers, 777 ± 140 in non- pmol/l in controls. Peak enterogl were significantly ($p < 0.05$) higher pmol/l), compared to non-dumper trols (104 ± 26 pmol/l). There was tween integrated GLP-1 and integ $p < 0.001$). The median emptying ha tric substitute was 480 sec, 352 ± 1(635 ± 131 sec in non-dumpers. The related inversely with integrated (and insulin ($p < 0.01$). Gel filtrati pooled postprandial plasma of gast revealed that all glucagon-like imm K_d 0.30, the elution position of glic GLP-1 like immunoreactivity elute position of gut GLP-1. The author known hyperinsulinemia after parti is induced by GLP-1. It seems like unabsorbed nutrients stimulates the the distal small bowel.

195 Erythromycin Exerts a Prokin with Chronic Idiopathic Intest Obstruction

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Chronic idiopathic intestin (CIIP) is a disease with diverse etiol presentation, felt to be related to vis ropathy. Erythromycin (E) induces migrating motility complex (MMC) gering the motilin receptor without We compared the effect of i.v. E (l on interdigestive gastroduodenal m CIIP vs. 6 controls, using an 8 lume metric recording technique. Phase controls was: number of gastric (M ± SEM), duration 6.0 ± 0.7 mi contractions 45.[illegible] ± 3.32, duration CIIP patients had no organized mot E induced a burst of strong, rhythm all subjects which migrated to the d MMC in 2/6 controls and 3/3 patient ence was observed in num CIIP = 22.6 ± 7.5) or durat CIIP = 12.8 ± 1.9) of gastric contr E.E (3.5 mg/kg) induces phase 3 of M duodenum of patients with CIIP. T therapeutic possibilities for some p

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